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Notice of Allowability	Application No.	Applicant(s)	
	10/828,353	JOHNSON, MICHAEL R.	
	Examiner	Art Unit	
	Zachary C. Tucker	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--
 All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☐ This communication is responsive to _____.
2. ☒ The allowed claim(s) is/are 82-115.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|--|
| <ol style="list-style-type: none"> 1. <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date <u>21Apr04,20Mar06</u> 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material | <ol style="list-style-type: none"> 5. <input type="checkbox"/> Notice of Informal Patent Application 6. <input type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date _____. 7. <input type="checkbox"/> Examiner's Amendment/Comment 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance 9. <input type="checkbox"/> Other _____. |
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Preliminary Amendments

The preliminary amendments filed on 21 April and 4 November 2004, requesting changes to the specification and claims, have been entered.

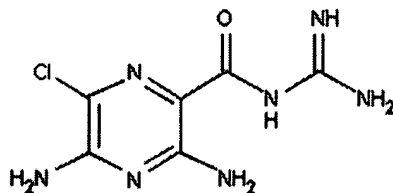
Allowable Subject Matter

Claims 82-115 are allowed.

The following is an examiner's statement of reasons for allowance:

The compounds, the composition and the method according to the allowed claims are novel and unobvious over the prior art.

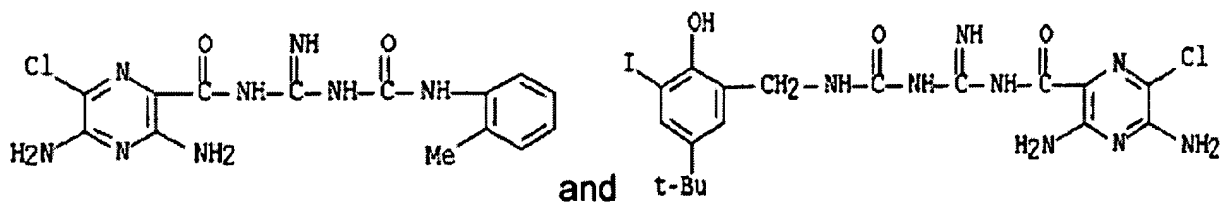
In the prior art, many derivatives of the drug amiloride have been known for a long time. Compounds of the present invention are based on a core structure of the compound amiloride, which has this structure:



Amiloride was first disclosed in US 3,313,813 (Cragoe, Jr.).

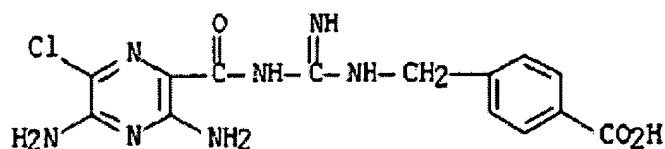
Derivatives of amiloride have been disclosed, where the guanidyl hydrogens are functionalized with alkylphenyl groups, wherein the phenyl is further substituted with halogen, methyl or amino groups. Such compounds, for example, are known from US 4,085,211 (Cragoe, Jr. et al), which describes compounds of the following structures (appearing on the next page):

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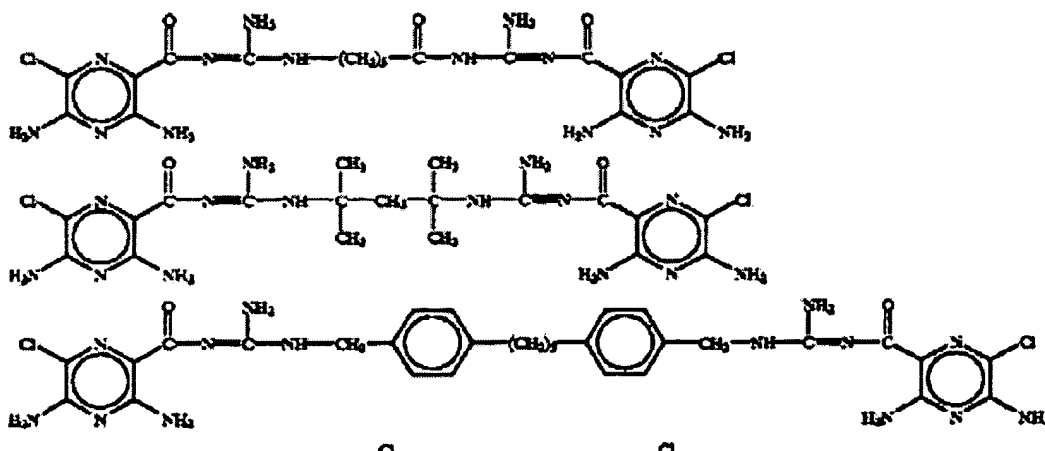


Another prior art disclosure of note is Kleyman et al, "Distinct epitopes on amiloride.

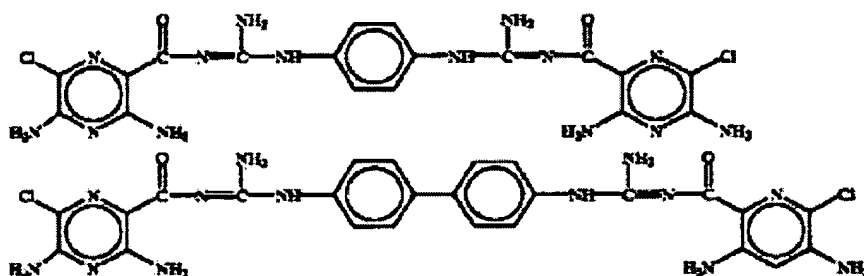
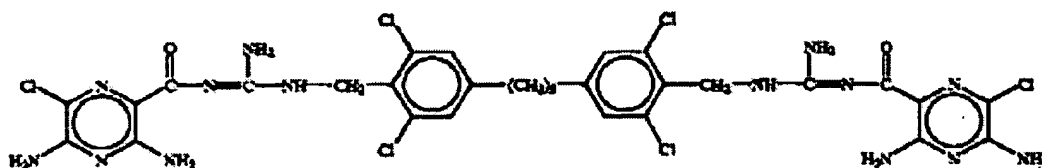
II. Variably restricted epitopes defined by monoclonal anti-amiloride antibodies" American Journal of Physiology, vol. 260(2, Pt. 1), pages C271-C276 (1991), which reports a compound having this structure:



US 6,475,509 (Boucher, Jr. et al) is pertinent for its disclosure of *bis*-amiloride compounds having the following structural formulae, none of which is within the scope of any of the presently allowed claims:



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Another particularly pertinent disclosure is Velly et al, "Effects of amiloride and its analogues on [3H]batrachotoxinin-A 20- α benzoate binding, [3H]tetracaine binding and 22 Na influx" European Journal of Pharmacology, vol. 149, no- 1-2, 1988, pages 97-105. Velly et al reports several derivatives of amiloride, which are not disclosed in any of the other references, cited hereinabove. Structures of these compounds are shown in Table I on page 99 of the reference.

A compound according to the present invention must have three nitrogen atoms in the "Q" containing ring as shown in formula (I) of instant claim 82, providing for 1,2,4- and 1,3,5-triazine rings, which provide for novel compounds over the prior art.

This reference:

Kellerman, D. "P2Y2 Receptor Agonists. A New Class of Medication Targeted at Improved Mucociliary Clearance" Chest, vol. 121(5), supplement, pages 201S-205S.

Has been cited by the examiner to show that one of ordinary skill understood the

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scope of claim 113, wherein a compound according to the present invention and a P2Y2 agonist are specified together as active ingredients in a pharmaceutical composition.

Insofar as applicant's other issued U.S. patents disclosing and claiming sodium channel blocker compounds based on the same core amiloride motif, none of those patents poses any double patenting issues with respect to the instant claims, although the language of the method claims in these issued patents is the same, the compounds with which the methods are practiced are different. There is no overlap between any of the instantly claimed subject matter and subject matter claimed in applicant's other patents in the present series.

These issued patents are:

US 6,858,614, US 6,828,615, US 6,903,105, US 6,995,160, US 7,026,325, US 7,030,117 and US 7,064,129.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

All Post-Allowance Correspondence concerning this application must be mailed to:
Mail Stop Issue Fee
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Or you can fax them to the Office of Patent Publications at 703-872-9306, in order to expedite the handling of such correspondence as amendments under 37 CFR 1.312; information disclosure statements, and formal drawings. Sending Post-Allowance papers to Technology Center 1600 will only cause delays in matching papers with the case.

For information concerning status of correspondence sent after receipt of the Notice of Allowance, please contact the Correspondence Branch at (703) 305-8027. The Notice

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of Allowance also has an insert containing contact information on other items, including Issue Fees, receipt of formal drawings and the status of the application.

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A handwritten signature in black ink, appearing to be "Z. Chen", with a long horizontal line extending to the right.